

REMARKS

1. Preliminary Remarks

a. Status of the Claims

Claims 1-32 are pending in this application. Claims 1, 10, 20, 23 and 26 are amended. Claim 5 is withdrawn as being directed to a non-elected invention. Claims 2, 9, 14, 16, 19, 24, 27, and 28 are canceled. Claims 30-32 are new.

b. Amendment of the Claims

In order to expedite prosecution and without prejudice to seeking claims of similar scope in a continuing application, claims 2, 9, 14, 16, 19, 24, 27 and 28 are canceled. Claim 1 is amended to address allegedly improper markush groups. Claim 26 is amended to be directed to a method for treating a medical disorder selected from the group consisting of Parkinson's disease, schizophrenia, cognitive disturbances, depression, anxiety, addiction, kidney function disturbances, and eating disturbances comprising administering to a subject in need thereof an effective amount of at least one compound of claim 1. Support for claim 26 can be found throughout the specification, for example, pages 51-53. Claim 23 is amended to simply provide a period at the end of the claim and not for any reasons of patentability. Claim 10 is amended to depend from claim 1 rather than claim 9 as claim 9 is canceled. Claim 20 is amended to depend from claim 15 rather than canceled claim 19. New claims 29-32 are further subspecies of the compound of general formula I-Aa. Support for new claims 29-32 can be found throughout the specification, for example, pages 20 and 21.

c. Improper Markush Rejection

On page 3 of the Office Action, the Examiner rejects claims 1-4 and 6-32 under a judicially created doctrine as being drawn to an improper Markush group where the claims lack unity of invention. In response, Applicant has amended claim 1 to remove the improper Markush groups thereby rendering the rejection moot.

2. Patentability Remarks

a. 35 U.S.C. §112, second paragraph

On pages 3 and 4 of the Office Action, the Examiner rejects claims 1-4 and 6-32 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite.

"General"

On page 4, part (i), the Examiner asserts that the term “general” in claim 1 renders the claim indefinite because it implies more than what is positively recited in the claims. Applicant has amended claim 1 to remove the term “general” thereby rendering the rejection moot.

“Substituted”

On page 4, part (ii), the Examiner asserts that the term “substituted” is indefinite as it is unclear which substituents are intended. Applicant has amended the claims to define the substituents. For example, in claim 1, optionally substituted alkyl and optionally substituted phenyl are defined near the end of the claim. Applicant submits the amendments overcome the alleged indefiniteness of the term “substituted.”

“Heterocycle”

On page 4, part (iii), the Examiner asserts that the term heterocycle is indefinite because it is not known how many atoms make up the ring. Applicant respectfully traverses. The term



“heterocycle” in claim 1 is associated with (hereafter the “NZ ring”), which defines a number of the ring members. Specifically, the NZ ring defines a five to eight members for monocyclic ring and 7 to 121 members if the ring is bicyclic. Also, the NZ ring is defined by the degree of unsaturation (from monosaturated if the ring is monocyclic to saturated if the ring is bicyclic). The NZ ring is also defined by the possible number and type of heteroatoms, namely 1 nitrogen atom and optionally a further heteroatom selected from O, S, or N. The other “heterocycles” have been similarly defined in claim 1 again by the kind of ring (monocyclic or bicyclic), saturated or unsaturated, fused or unfused, and the type and number of heteroatoms in the heterocyclic ring. In view of the foregoing, Applicant submits that the claims set forth the subject matter that the Applicant regards as their invention and particularly point out and distinctly define the metes and bounds of the subject matter to be patented.

“Optionally”

On page 4, part (iv), the Examiner asserts the term “optionally” in claim 25 should be deleted because a pharmaceutical composition necessarily requires the presence of a carrier. Applicant is grateful to the Examiner for the suggestion and submits that claim 25 has been amended to delete the term “optionally” thereby rendering the rejection moot. In view of the foregoing amendment and remarks, Applicant submits that the rejection of claims 1-4 and 6-32 under 35 U.S.C. §112, second paragraph, has been overcome and should be withdrawn.

b. 35 U.S.C. §112, first paragraph

On pages 4 and 5 of the Office Action, the Examiner rejects claims 26-28 under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the Examiner asserts that the Applicant has failed to provide what disease or symptom is being treated, who the subject being treated for, or the particular dosing regimen or mode of administration. The Examiner asserts that CNS disorders and similarly kidney function disorders are due to different cause and different treatments. Accordingly, the Examiner concludes that the claimed subject matter is not described in the specification in such a way to enable one of skill in the art to make or use the invention.

Researchers have recognized the use of D3 receptor antagonists to treat Parkinson's Disease (PD). Specifically, the literature states that "elevations of the D3 receptor occur in schizophrenia and in experimental conditions of hyperdopaminergic tone... which also may occur with L-dopa-induced dyskinesias in PD. Thus, D3 receptor antagonists could prove to be effective in the treatment of schizophrenia, psychostimulant drug abuse, and drug-induced dyskinesias..." J.N. Joyce. *Pharmacology and Therapeutics*, 2001;90:231-59 ("Joyce" hereafter) at pages 251-2. Joyce also discloses that, "[an] effective antiparkinsonian D3-preferring agonist... [exhibits] antidepressive effects," and that, "experimental models of PD suggest that D3-preferring agonists do act through D3 receptors to provide relief of akinesia." Joyce at pages 251-2 (emphasis added). Accordingly, researchers recognized that dopamine D3 receptor-targeting drugs could be used to treat disorders including PD, schizophrenia, depression, and others.

Further, improvements in learning performance have been observed with treatment using various D3 receptor antagonists in a rat model of scopolamine-induced amnesia, which models cognitive dysfunction. See J.Laszy et al. *Psychopharmacology*, 2005;179:567-75. Additionally, drug addiction has been shown to be attenuated in a rat model by D3 receptor blockade via D3 receptor antagonists. See C.A. Heidbredder et al. *Brain Research Reviews*, 2005;49:77-105. Antianxiety effects in a rat model have also been demonstrated for dopamine D3 receptor-targeting drugs. See Z. Rogóż et al., *Polish Journal of Pharmacology*, 2003;55:449-54. Additionally, D3 receptors have been implicated in regulating renal function. See Mühlbauer et al., *Acta Physiologica Scandinavica*, 2000;168(1):219-23. Moreover, given that dopamine D3 receptor-/- mice exhibit increased levels of body fat compared to wild-type when fed a high fat diet, the role of the dopamine system in mediating changes of food intake elicited by metabolic and adiposity signals has been explored. See Benoit et al., *Behavioral Neuroscience*, 2003;117(1):46-54 ("Benoit"). Benoit shows that D3 receptor

/- mice were hyperresponsive to amylin and leptin compared to wild-type, and that the D3 receptor chronically inhibits the effects of adiposity hormones, contributes to a net anabolic state, and plays a central role in eating disturbances. All of these references indicate that rather than being groundless, the evidentiary connection between the instantly claimed compounds and their potential use for treating PD, cognitive disturbances, addiction, anxiety, kidney function disorders, and eating disturbances was sufficiently studied and would be convincing to one of ordinary skill in the art regarding how the claimed compound might be used to treat the conditions claimed in amended claim 17. Applicant respectfully submits this evidence merely needs to be convincing rather than conclusive to one of skill in the art. See MPEP §2164.05 and *In re Brandstadter*, 482 F.2d. 1935 (CCPA 1973). Applicant further submits that based on the prior art, one of ordinary skill in the art could have anticipated the effects of D3 receptor agonists on the medical conditions of amended claim 26.

In view of the teachings of the instant written description, and the art described above, Applicant submits that the instant written description is enabled because one of ordinary skill in the art could readily have anticipated the effects of a change within the claimed subject matter. See MPEP § 2164.03. Although some experimentation might have been necessary to establish the extent of the usefulness of the instantly claimed compound, the instantly claimed subject matter was enabled because one of ordinary skill in the art had sufficient direction and guidance from the instant written description as to how to use the compound to treat the conditions of amended claim 17—determining whether the extent to which the instantly claimed compound treats these conditions was routine, as demonstrated by the references described above. See MPEP § 2164.05. In view of the foregoing amendments and remarks, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 112, first paragraph.

3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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